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# THE CONCISE GUIDE TO PHARMACOLOGY 2015/16: Overview

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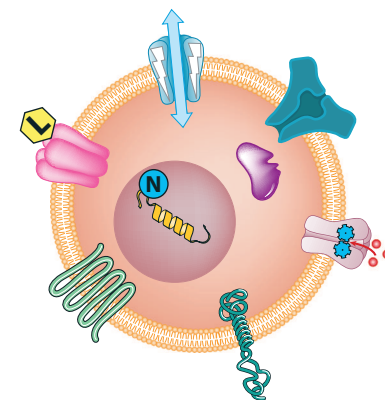
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## Abstract

The Concise Guide to PHARMACOLOGY 2015/16 provides concise overviews of the key properties of over 1750 human drug targets with their pharmacology, plus links to an open access knowledgebase of drug targets and their ligands ([www.guidetopharmacology.org](http://www.guidetopharmacology.org)), which provides more detailed views of target and ligand properties. The full contents can be found at <http://onlinelibrary.wiley.com/doi/10.1111/bph.13347/full>. This compilation of the major pharmacological targets is divided into eight areas of focus: G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, other ion channels, nuclear hormone receptors, catalytic receptors, enzymes and transporters. These are presented with nomenclature guidance and summary information on the best available pharmacological tools, alongside key references and suggestions for further reading. The Concise Guide is published in landscape format in order to facilitate comparison of related targets. It is a condensed version of material contemporary to late 2015, which is presented in greater detail and constantly updated on the website [www.guidetopharmacology.org](http://www.guidetopharmacology.org), superseding data presented in the previous Guides to Receptors & Channels and the Concise Guide to PHARMACOLOGY 2013/14. It is produced in conjunction with NC-IUPHAR and provides the official IUPHAR classification and nomenclature for human drug targets, where appropriate. It consolidates information previously curated and displayed separately in IUPHAR-DB and GRAC and provides a permanent, citable, point-in-time record that will survive database updates.

## Table of contents

### 5729 Overview

5734 Other Protein Targets

5734 Adiponectin receptors

5735 Blood coagulation components

5735 Non-enzymatic BRD containing proteins

5736 Carrier proteins

5737 CD molecules

5738 Methyllysine reader proteins

5739 Cytokines and growth factors

5739 Fatty acid-binding proteins

5741 Sigma receptors

5742 Tubulins

### 5744 G protein-coupled receptors

5746 Orphan and other 7TM receptors

5746 Class A Orphans

5756 Class C Orphans

5756 Taste 1 receptors

5757 Taste 2 receptors

5758 Other 7TM proteins

5759 5-Hydroxytryptamine receptors

5764 Acetylcholine receptors (muscarinic)

5766 Adenosine receptors

5768 Adhesion Class GPCRs

5770 Adrenoceptors

5774 Angiotensin receptors

5775 Apelin receptor

5777 Bile acid receptor  
 5778 Bombesin receptors  
 5780 Bradykinin receptors  
 5781 Calcitonin receptors  
 5783 Calcium-sensing receptors  
 5784 Cannabinoid receptors  
 5785 Chemerin receptor  
 5785 Chemokine receptors  
 5791 Cholecystokinin receptors  
 5792 Class Frizzled GPCRs  
 5793 Complement peptide receptors  
 5795 Corticotropin-releasing factor receptors  
 5796 Dopamine receptors  
 5798 Endothelin receptors  
 5799 G protein-coupled estrogen receptor  
 5800 Formylpeptide receptors  
 5801 Free fatty acid receptors  
 5803 GABAB receptors  
 5805 Galanin receptors  
 5806 Ghrelin receptor  
 5807 Glucagon receptor family  
 5809 Glycoprotein hormone receptors  
 5810 Gonadotrophin-releasing hormone receptors  
 5811 GPR18, GPR55 and GPR119  
 5812 Histamine receptors  
 5814 Hydroxycarboxylic acid receptors  
 5815 Kisspeptin receptor  
 5816 Leukotriene receptors  
 5818 Lysophospholipid (LPA) receptors  
 5819 Lysophospholipid (SIP) receptors  
 5820 Melanin-concentrating hormone receptors  
 5821 Melanocortin receptors  
 5822 Melatonin receptors  
 5823 Metabotropic glutamate receptors  
 5826 Motilin receptor  
 5827 Neuromedin U receptors  
 5828 Neuropeptide FF/neuropeptide AF receptors  
 5829 Neuropeptide S receptor  
 5828 Neuropeptide W/neuropeptide B receptors  
 5830 Neuropeptide Y receptors  
 5832 Neurotensin receptors  
 5833 Opioid receptors  
 5835 Orexin receptors  
 5836 Oxoglutarate receptor  
 5836 P2Y receptors  
 5838 Parathyroid hormone receptors  
 5839 Platelet-activating factor receptor  
 5840 Prokineticin receptors  
 5841 Prolactin-releasing peptide receptor  
 5842 Prostanoid receptors

5844 Proteinase-activated receptors  
 5846 QRFPR receptor  
 5846 Relaxin family peptide receptors  
 5848 Somatostatin receptors  
 5850 Succinate receptor  
 5850 Tachykinin receptors  
 5852 Thyrotropin-releasing hormone receptors  
 5852 Trace amine receptor  
 5854 Urotensin receptor  
 5854 Vasopressin and oxytocin receptors  
 5856 VIP and PACAP receptors

**5870 Ligand-Gated Ion Channels**

5871 5-HT<sub>3</sub> receptors  
 5873 Acid-sensing (proton-gated) ion channels (ASICs)  
 5875 Epithelial sodium channels (ENaC)  
 5877 GABAA receptors  
 5882 Glycine receptors  
 5885 Ionotropic glutamate receptors  
 5891 IP<sub>3</sub> receptor  
 5891 Nicotinic acetylcholine receptors  
 5896 P2X receptors  
 5898 Ryanodine receptor  
 5900 ZAC

**5904 Voltage-gated ion channels**

5905 CatSper and Two-Pore channels  
 5907 Cyclic nucleotide-regulated channels  
 5909 Potassium channels  
 5910 Calcium-activated potassium channels  
 5912 Inwardly rectifying potassium channels  
 5915 Two-P potassium channels  
 5917 Voltage-gated potassium channels  
 5920 Transient Receptor Potential channels  
 5934 Voltage-gated calcium channels  
 5936 Voltage-gated proton channel  
 5937 Voltage-gated sodium channels

**5942 Other ion channels**

5943 Aquaporins  
 5944 Chloride channels  
 5944 CIC family  
 5947 CFTR  
 5948 Calcium activated chloride channel  
 5949 Maxi chloride channel  
 5950 Volume regulated chloride channels  
 5952 Connexins and Pannexins  
 5954 Sodium leak channel, non-selective

**5956 Nuclear hormone receptors**

5958 1A. Thyroid hormone receptors  
 5959 1B. Retinoic acid receptors  
 5960 1C. Peroxisome proliferator-activated receptors  
 5961 1D. Rev-Erb receptors  
 5962 1F. Retinoic acid-related orphans  
 5963 1H. Liver X receptor-like receptors  
 5964 1I. Vitamin D receptor-like receptors  
 5965 2A. Hepatocyte nuclear factor-4 receptors  
 5966 2B. Retinoid X receptors  
 5967 2C. Testicular receptors  
 5968 2E. Tailless-like receptors  
 5969 2F. COUP-TF-like receptors  
 5970 3B. Estrogen-related receptors  
 5971 4A. Nerve growth factor 1B-like receptors  
 5972 5A. Fushi tarazu F1-like receptors  
 5973 6A. Germ cell nuclear factor receptors  
 5974 0B. DAX-like receptors  
 5975 Steroid hormone receptors  
 5975 3A. Estrogen receptors  
 5976 3C. 3-Ketosteroid receptors

**5979 Catalytic receptors**

5981 Cytokine receptor family  
 5981 IL-2 receptor family  
 5983 IL-3 receptor family  
 5983 IL-6 receptor family  
 5985 IL-12 receptor family  
 5985 Prolactin receptor family  
 5986 Interferon receptor family  
 5987 IL-10 receptor family  
 5988 Immunoglobulin-like family of IL-1 receptors  
 5989 IL-17 receptor family  
 5990 GDNF receptor family  
 5991 Integrins  
 5994 Natriuretic peptide receptor family  
 5996 Pattern recognition receptors  
 5996 Toll-like receptor family  
 5997 NOD-like receptor family  
 5999 Receptor serine/threonine kinase (RSTK) family  
 6000 Type I receptor serine/threonine kinases  
 6001 Type II receptor serine/threonine kinases  
 6001 Type III receptor serine/threonine kinases  
 6002 RSTK functional heteromers  
 6003 Receptor tyrosine kinases  
 6004 Type I RTKs: ErbB (epidermal growth factor) receptor family  
 6005 Type II RTKs: Insulin receptor family  
 6005 Type III RTKs: PDGFR, CSFR, Kit, FLT3 receptor family  
 6007 Type IV RTKs: VEGF (vascular endothelial growth factor)

receptor family	6040 M19: Membrane dipeptidase	6079 Lipoxygenases
6008 Type V RTKs: FGF (fibroblast growth factor) receptor family	6040 S1: Chymotrypsin	6080 Leukotriene and lipoxin metabolism
6008 Type VI RTKs: PTK7/CCK4	6041 T1: Proteasome	6081 GABA turnover
6009 Type VII RTKs: Neurotrophin receptor/Trk family	6042 S8: Subtilisin	6082 Glycerophospholipid turnover
6010 Type VIII RTKs: ROR family	6042 S9: Prolyl oligopeptidase	6082 Phosphatidylinositol kinases
6010 Type IX RTKs: MuSK	6042 Acetylcholine turnover	6083 1-phosphatidylinositol 4-kinase family
6010 Type X RTKs: HGF (hepatocyte growth factor) receptor family	6044 Adenosine turnover	6083 Phosphatidylinositol-4-phosphate 3-kinase family
6011 Type XI RTKs: TAM (TYRO3-, AXL- and MER-TK) receptor family	6045 Amino acid hydroxylases	6084 Phosphatidylinositol 3-kinase family
6012 Type XII RTKs: TIE family of angiopoietin receptors	6046 L-Arginine turnover	6084 Phosphatidylinositol-4,5-bisphosphate 3-kinase family
6012 Type XIII RTKs: Ephrin receptor family	6047 Arginase	6085 1-phosphatidylinositol-3-phosphate 5-kinase family
6013 Type XIV RTKs: RET	6047 Arginine:glycine amidinotransferase	6085 Type I PIP kinases (1-phosphatidylinositol-4-phosphate 5-kinase family)
6014 Type XV RTKs: RYK	6047 Dimethylarginine dimethylaminohydrolases	6086 Type II PIP kinases (1-phosphatidylinositol-5-phosphate 4-kinase family)
6014 Type XVI RTKs: DDR (collagen receptor) family	6048 Nitric oxide synthases	6087 Phosphoinositide-specific phospholipase C
6015 Type XVII RTKs: ROS receptors	6048 Carboxylases and decarboxylases	6088 Phospholipase A <sub>2</sub>
6015 Type XVIII RTKs: LMR family	6049 Carboxylases	6089 Phosphatidylcholine-specific phospholipase D
6016 Type XIX RTKs: Leukocyte tyrosine kinase (LTK) receptor family	6050 Decarboxylases	6090 Lipid phosphate phosphatases
6016 Type XX RTKs: STYK1	6052 Catecholamine turnover	6091 Haem oxygenase
6017 Receptor tyrosine phosphatases (RTP)	6055 Ceramide turnover	6092 Hydrogen sulphide synthesis
6018 Tumour necrosis factor (TNF) receptor family	6055 Serine palmitoyltransferase	6093 Hydrolases
	6056 Ceramide synthase	6093 Inositol phosphate turnover
<b>6024 Enzymes</b>	6057 Sphingolipid $\Delta^4$ -desaturase	6094 Inositol 1,4,5-trisphosphate 3-kinases
6028 Protein Kinases (EC 2.7.x.x)	6058 Sphingomyelin synthase	6094 Inositol polyphosphate phosphatases
6028 Rho kinase	6058 Sphingomyelin phosphodiesterase	6094 Inositol monophosphatase
6029 Protein kinase C (PKC)	6059 Neutral sphingomyelinase coupling factors	6095 Lanosterol biosynthesis pathway
6029 Alpha subfamily	6059 Ceramide glucosyltransferase	6097 Nucleoside synthesis and metabolism
6029 Delta subfamily	6060 Acid ceramidase	6099 Sphingosine 1-phosphate turnover
6030 Eta subfamily	6060 Neutral ceramidases	6100 Sphingosine kinase
6030 FRAP subfamily	6061 Alkaline ceramidases	6100 Sphingosine 1-phosphate phosphatase
6031 CDK4 subfamily	6061 Ceramide kinase	6101 Sphingosine 1-phosphate lyase
6031 GSK subfamily	6062 Chromatin modifying enzymes	6101 Thyroid hormone turnover
6032 Polo-like kinase (PLK) family	6062 2.1.1.- Protein arginine N-methyltransferases	6103 1.14.11.29 2-oxoglutarate oxygenases
6032 STE7 family	6062 3.5.1.- Histone deacetylases (HDACs)	6103 2.4.2.30 poly(ADP-ribose)polymerases
6033 Abl family	6063 Cyclic nucleotide turnover	6104 2.5.1.58 Protein farnesyltransferase
6033 Ack family	6063 Adenylyl cyclases	6104 3.5.3.15 Peptidyl arginine deiminases (PADI)
6034 Janus kinase (JakA) family	6064 Soluble guanylyl cyclase	6104 RAS subfamily
6034 Src family	6065 Exchange protein activated by cyclic AMP (Epac)	6105 4.2.1.1 Carbonate dehydratases
6035 Tec family	6066 Phosphodiesterases, 3',5'-cyclic nucleotide	6105 5.99.1.2 DNA Topoisomerases
6035 RAF family	6069 Cytochrome P450	
6036 Peptidases and proteinases	6069 CYP1 family	
6036 A1: Pepsin	6070 CYP2 family	
6037 A22: Presenilin	6070 CYP3 family	
6037 C14: Caspase	6071 CYP4 family	
6037 M1: Aminopeptidase N	6072 CYP5, CYP7 and CYP8 families	
6038 M2: Angiotensin-converting (ACE and ACE2)	6072 CYP11, CYP17, CYP19, CYP20 and CYP21 families	
6038 M10: Matrix metalloproteinase	6073 CYP24, CYP26 and CYP27 families	
6039 M12: Astacin/Adamalysin	6074 CYP39, CYP46 and CYP51 families	
6039 M28: Aminopeptidase Y	6075 Endocannabinoid turnover	
	6076 Eicosanoid turnover	
	6077 Cyclooxygenase	
	6077 Prostaglandin synthases	
		<b>6110 Transporters</b>
		6113 ATP-binding cassette transporter family
		6113 ABCA subfamily
		6115 ABCB subfamily
		6116 ABCC subfamily
		6117 ABCD subfamily of peroxisomal ABC transporters
		6118 ABCG subfamily
		6119 F-type and V-type ATPases
		6119 F-type ATPase
		6120 V-type ATPase

6120	P-type ATPases	6145	SLC10 family of sodium-bile acid co-transporters	6172	SLC27 family of fatty acid transporters
6121	Na <sup>+</sup> /K <sup>+</sup> -ATPases	6147	SLC11 family of proton-coupled metal ion transporters	6173	SLC28 and SLC29 families of nucleoside transporters
6121	Ca <sup>2+</sup> -ATPases	6148	SLC12 family of cation-coupled chloride transporters	6173	SLC28 family
6122	H <sup>+</sup> /K <sup>+</sup> -ATPases	6149	SLC13 family of sodium-dependent sulphate/carboxylate transporters	6174	SLC29 family
6122	Cu <sup>+</sup> -ATPases	6150	SLC14 family of facilitative urea transporters	6176	SLC30 zinc transporter family
6122	Phospholipid-transporting ATPases	6151	SLC15 family of peptide transporters	6176	SLC31 family of copper transporters
6123	Major facilitator superfamily (MFS) of transporters	6152	SLC16 family of monocarboxylate transporters	6177	SLC32 vesicular inhibitory amino acid transporter
6123	SLC superfamily of solute carriers	6154	SLC17 phosphate and organic anion transporter family	6178	SLC33 acetylCoA transporter
6124	SLC1 family of amino acid transporters	6154	Type I sodium-phosphate co-transporters	6179	SLC34 family of sodium phosphate co-transporters
6124	Glutamate transporter subfamily	6155	Sialic acid transporter	6180	SLC35 family of nucleotide sugar transporters
6126	Alanine/serine/cysteine transporter subfamily	6155	Vesicular glutamate transporters (VGLUTs)	6181	SLC36 family of proton-coupled amino acid transporters
6127	SLC2 family of hexose and sugar alcohol	6156	Vesicular nucleotide transporter	6182	SLC37 family of phosphosugar/phosphate exchangers
6127	Class I transporters	6156	SLC18 family of vesicular amine transporters	6182	SLC38 family of sodium-dependent neutral amino acid transporters
6128	Class II transporters	6158	SLC19 family of vitamin transporters	6183	System A-like transporters
6129	Proton-coupled inositol transporter	6159	SLC20 family of sodium-dependent phosphate transporters	6183	System N-like transporters
6129	SLC3 and SLC7 families of heteromeric amino acid transporters (HATs)	6160	SLC22 family of organic cation and anion transporters	6184	Orphan SLC38 transporters
6130	SLC3 family	6160	Organic cation transporters (OCT)	6185	SLC39 family of metal ion transporters
6130	SLC7 family	6161	Organic zwitterions/cation transporters (OCTN)	6186	SLC40 iron transporter
6131	SLC4 family of bicarbonate transporters	6162	Organic anion transporters (OATs)	6187	SLC41 family of divalent cation transporters
6132	Anion exchangers	6163	Urate transporter	6187	SLC42 family of Rhesus glycoprotein ammonium transporters
6132	Sodium-dependent HCO <sub>3</sub> <sup>-</sup> transporters	6163	SLC23 family of ascorbic acid transporters	6188	SLC43 family of large neutral amino acid transporters
6133	SLC5 family of sodium-dependent glucose transporters	6164	SLC24 family of sodium/potassium/calcium exchangers	6189	SLC44 choline transporter-like family
6134	Hexose transporter family	6165	SLC25 family of mitochondrial transporters	6190	SLC45 family of putative sugar transporters
6135	Choline transporter	6165	Mitochondrial di- and tri-carboxylic acid transporter subfamily	6191	SLC46 family of folate transporters
6136	Sodium iodide symporter, sodium-dependent multivitamin transporter and sodium-coupled monocarboxylate transporters	6166	Mitochondrial amino acid transporter subfamily	6192	SLC47 family of multidrug and toxin extrusion transporters
6137	Sodium <i>myo</i> -inositol cotransporter transporters	6167	Mitochondrial phosphate transporters	6192	SLC48 heme transporter
6138	SLC6 neurotransmitter transporter family	6167	Mitochondrial nucleotide transporter subfamily	6193	SLC49 family of FLVCR-related heme transporters
6138	Monoamine transporter subfamily	6168	Mitochondrial uncoupling proteins	6194	SLC50 sugar transporter
6139	GABA transporter subfamily	6169	Miscellaneous SLC25 mitochondrial transporters	6195	SLC51 family of steroid-derived molecule transporters
6141	Glycine transporter subfamily	6170	SLC26 family of anion exchangers	6195	SLC52 family of riboflavin transporters
6142	Neutral amino acid transporter subfamily	6170	Selective sulphate transporters	6196	SLCO family of organic anion transporting polypeptides
6144	SLC8 family of sodium/calcium exchangers	6170	Chloride/bicarbonate exchangers	6199	Patched family
6145	SLC9 family of sodium/hydrogen exchangers	6171	Anion channels		
		6171	Other SLC26 anion exchangers		

## Introduction

In order to allow clarity and consistency in pharmacology, there is a need for a comprehensive organisation and presentation of the targets of drugs. This is the philosophy of the IUPHAR/BPS Guide to PHARMACOLOGY presented on the online free access database (<http://www.guidetopharmacology.org/>). This database is supported by the British Pharmacological Society (BPS), the International Union of Basic and Clinical Pharmacology (IUPHAR), the Wellcome Trust and the University of Edinburgh. Data included in the Guide to PHARMACOLOGY are derived in large part from interactions with the subcommittees of the Nomenclature

Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR). The Editors of the Concise Guide have compiled the individual records, in concert with the team of Curators, drawing on the expert knowledge of these latter subcommittees. The tables allow an indication of the status of the nomenclature for the group of targets listed, usually previously published in Pharmacological Reviews. In the absence of an established subcommittee, advice from several prominent, independent experts has generally been obtained to produce an authoritative consensus on nomenclature, which attempts to fit in within the gen-

eral guidelines from NC-IUPHAR. This current edition, the Concise Guide to PHARMACOLOGY 2015/16, is the latest snapshot of the database in print form, following on from the Concise Guide to PHARMACOLOGY 2013/14. It contains data drawn from the online database as a rapid overview of the major pharmacological targets. Thus, there are fewer targets presented in the Concise Guide (1761) compared to the online database (2761, as of August 2015). The priority for inclusion in the Concise Guide is the presence of quantitative pharmacological data. This means that often orphan family members are not presented in the Con-



cise Guide, although structural information is available on the on-line database. An expansion in the current version of the Concise Guide is the increased inclusion of approved drugs, which reflects the aim of the online database to reflect the clinical exploitation of human molecular targets. Although many of these agents are much less selective than the tool compounds listed to define individual targets or groups of targets, we have included them for the significant interest associated with their use and mechanisms of action. The emphasis on approved drugs means that the online database has been expanded to include 8024 ligands (as of August 2015), meaning that additional records now appear in the Concise Guide, primarily in the enzymes section. The organisation of the data is tabular (where appropriate) with a standardised format, where possible on a single page, intended to aid understanding of and comparison within a particular target group. The Concise Guide is intended as an initial resource, with links to additional

reviews and resources for greater depth and information. Pharmacological and structural data focus primarily on human gene products, wherever possible, with links to HGNC gene nomenclature and UniProt IDs. In a few cases, where data from human proteins are limited, data from other species are indicated. Pharmacological tools listed are prioritised on the basis of selectivity and availability. That is, agents (agonists, antagonists, inhibitors, activators, etc.) are included where they are both available (by donation or from commercial sources, now or in the near future) AND the most selective. This edition of the Concise Guide is divided into nine sections, which comprise pharmacological targets of similar structure/function. These are G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, other ion channels, catalytic receptors, nuclear hormone receptors, enzymes, transporters and other protein targets. A new aspect of the Concise Guide 2015/16 is that each of these sections contains a

complete listing of the families available for inspection on the on-line database, identifying those families reported in the Concise Guide by their page numbers. We hope that the Concise Guide will provide for researchers, teachers and students a state-of-the-art source of accurate, curated information on the background to their work that they will use in the Introductions to their Research Papers or Reviews, or in supporting their teaching and studies.

We recommend that any citations to information in the Concise Guide are presented in the following format:

Alexander SPH *et al.* (2015). The Concise Guide to PHARMACOLOGY 2015/16: Overview. *Br J Pharmacol* XXX.

In this overview are listed protein targets of pharmacological interest, which are not G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, ion channels, nuclear hormone receptors, catalytic receptors, transporters or enzymes.

#### A dedication

This Edition of the Concise Guide to PHARMACOLOGY is dedicated to Tony Harmar (1951–2014). Tony was a friend and colleague, who was involved with IUPHAR for over 15 years and worked on the IUPHAR database for over a decade at Edinburgh, working hard to establish the curators as a team

of highly informed and informative individuals imbued with Tony's passion and dogged determination to focus on high-quality data input, ensuring high-quality data output. With time and the resources of the BPS and Wellcome Trust, combined with the expertise of the NC-IUPHAR committee mem-

bers mentioned above, Tony established the online database at <http://www.guidetopharmacology.org/> as the exceptional resource it is today.

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#### Conflict of interest

The authors state that there are no conflicts of interest to disclose.

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# Other Protein Targets

## Family structure

5734	Adiponectin receptors	5739	Fatty acid-binding proteins	–	R4 family
–	B-cell lymphoma 2 (Bcl-2) protein family	–	Heat shock proteins	–	R7 family
5735	Blood coagulation components	–	Immunoglobulins	–	R12 family
–	Bromodomain-containing proteins	–	Inhibitors of apoptosis (IAP) protein family	–	Reticulons
5735	Non-enzymatic BRD containing proteins	–	Kelch-like proteins	–	Ribosomal factors
5736	Carrier proteins	–	Kinesins	5741	Sigma receptors
5737	CD molecules	–	Mitochondrial-associated proteins	5742	Tubulins
–	Chromatin-interacting transcriptional repressors	–	Notch receptors	–	Tumour-associated proteins
5738	Methyllysine reader proteins	–	Pentaxins	–	WD repeat-containing proteins
–	Circadian clock proteins	–	Serum pentaxins		
5739	Cytokines and growth factors	–	Regulators of G protein signaling (RGS) proteins		
–	EF-hand domain containing	–	RZ family		

# Adiponectin receptors

Other protein targets → Adiponectin receptors

**Overview:** Adiponectin receptors (**provisional nomenclature**, [ENSM00500000270960](#)) respond to the 30 kDa complement-related protein hormone adiponectin (also known as *ADIPOQ*: adipocyte, C1q and collagen domain-containing protein; ACRP30, adipose most abundant gene transcript 1; apM-1; gelatin-binding protein: [Q15848](#)) originally cloned from adipocytes [\[49\]](#). Although sequence data suggest 7TM domains,

immunological evidence indicates that, contrary to typical 7TM topology, the carboxyl terminus is extracellular, while the amino terminus is intracellular [\[86\]](#). Signalling through these receptors appears to avoid G proteins. Adiponectin receptors appear rather to stimulate protein phosphorylation via AMP-activated protein kinase and MAP kinase pathways [\[86\]](#), possibly through the protein partner *APPL1* (adaptor protein, phosphotyrosine in-

teraction, PH domain and leucine zipper containing 1, [Q9UKG1](#) [\[52\]](#)). The adiponectin receptors are a class of proteins (along with membrane progesterin receptors), which contain seven sequences of aliphatic amino acids reminiscent of GPCRs, but which are structurally and functionally distinct from that class of receptor.

Nomenclature	Adipo1 receptor	Adipo2 receptor
HGNC, UniProt	<i>ADIPOR1</i> , <a href="#">Q96A54</a>	<i>ADIPOR2</i> , <a href="#">Q86V24</a>
Rank order of potency	globular adiponectin ( <i>ADIPOQ</i> , <a href="#">Q15848</a> ) > adiponectin ( <i>ADIPOQ</i> , <a href="#">Q15848</a> )	globular adiponectin ( <i>ADIPOQ</i> , <a href="#">Q15848</a> ) = adiponectin ( <i>ADIPOQ</i> , <a href="#">Q15848</a> )

**Comments:** T-Cadherin ([CDH13](#), [P55290](#)) has also been suggested to be a receptor for (hexameric) adiponectin [\[35\]](#).

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# Blood coagulation components

Other protein targets → Blood coagulation components

**Overview:** Coagulation as a patho/physiological process is interpreted as a mechanism for reducing excessive blood loss through the generation of a gel-like clot local to the site of injury. The process involves the activation, adhesion (see [Integrins](#)), degradation and aggregation of platelets, as well as proteins circulating in the plasma. The coagulation cascade involves multiple proteins being converted to more active forms from less active precursors, typically through proteolysis (see [Proteases](#)). Listed here are the components of the coagulation cascade targeted by agents in current clinical usage.

Nomenclature	coagulation factor V (proaccelerin, labile factor)	coagulation factor VIII, procoagulant component	serpin peptidase inhibitor, clade C (antithrombin), member 1
HGNC, UniProt	<a href="#">F5</a> , P12259	<a href="#">F8</a> , P00451	<a href="#">SERPINC1</a> , P01008
Selective activators	–	–	heparin (pK <sub>d</sub> 7.8) [25], fondaparinux (pK <sub>d</sub> 7.5) [65], dalteparin [34], danaparoid [15, 58], enoxaparin [17], tinzaparin [19]
Selective antagonists	drotrecogin alfa (Inhibition) [40, 41]	drotrecogin alfa (Inhibition) [40, 41]	–

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# Non-enzymatic BRD containing proteins

Other protein targets → Bromodomain-containing proteins → Non-enzymatic BRD containing proteins

**Overview:** bromodomains bind proteins with acetylated lysine residues, such as histones, to regulate gene transcription. Listed herein are examples of bromodomain-containing proteins for which sufficient pharmacology exists.



Nomenclature	bromodomain adjacent to zinc finger domain, 2A	bromodomain adjacent to zinc finger domain, 2B	CREB binding protein	polybromo 1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4
HGNC, UniProt	<a href="#">BAZ2A</a> , <a href="#">Q9UIF9</a>	<a href="#">BAZ2B</a> , <a href="#">Q9UIF8</a>	<a href="#">CREBBP</a> , <a href="#">Q92793</a>	<a href="#">PBRM1</a> , <a href="#">Q86U86</a>	<a href="#">SMARCA4</a> , <a href="#">P51532</a>
Selective inhibitors	<a href="#">GSK2801</a> ( $pK_d$ 6.6) [ <a href="#">73</a> ]	<a href="#">GSK2801</a> (Binding) ( $pK_d$ 6.9) [ <a href="#">73</a> ]	<a href="#">I-CBP112</a> ( $pK_d$ 6.8) [ <a href="#">72</a> ]	<a href="#">PFI-3</a> (Binding) ( $pK_d$ 7.3) [ <a href="#">79</a> ]	<a href="#">PFI-3</a> (Binding) ( $pK_d$ 7.1) [ <a href="#">79</a> ]

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## Carrier proteins

Other protein targets → [Carrier proteins](#)

**Overview:** TTR is a homo-tetrameric protein which transports thyroxine in the plasma and cerebrospinal fluid and retinol (vitamin A) in the plasma. Many disease causing mutations in the protein have been reported, many of which cause complex dissociation and protein mis-assembly and deposition of toxic aggregates

amyloid fibril formation [66]. These amyloidogenic mutants are linked to the development of pathological amyloidoses, including familial amyloid polyneuropathy (FAP) [1, 13], familial amyloid cardiomyopathy (FAC) [37], amyloidotic vitreous opacities, carpal tunnel syndrome [57] and others. In old age, non-mutated TTR

can also form pathological amyloid fibrils [85]. Pharmacological intervention to reduce or prevent TTR dissociation is being pursued as a therapeutic strategy. To date one small molecule kinetic stabilising molecule (tafamidis) has been approved for FAP, and is being evaluated in clinical trials for other TTR amyloidoses.

Nomenclature	<a href="#">transthyretin</a>
Common abbreviation	TTR
HGNC, UniProt	<a href="#">TTR</a> , <a href="#">P02766</a>

## CD molecules

Other protein targets → CD molecules

**Overview:** Cluster of differentiation refers to an attempt to catalogue systematically a series of over 300 cell-surface proteins associated with immunotyping. Many members of the group have identified functions as enzymes (for example,

see [CD73 ecto-5'-nucleotidase](#)) or receptors (for example, see [CD41 integrin, alpha 2b subunit](#)). Many CDs are targetted for therapeutic gain using antibodies for the treatment of proliferative disorders. A full listing of all the Clusters of Differentiation is

not possible in the Guide to PHARMACOLOGY; listed herein are selected members of the family targetted for therapeutic gain.

Nomenclature	CD2	CD3e molecule, epsilon (CD3-TCR complex)	CD20 (membrane-spanning 4-domains, subfamily A, member 1)	CD33	CD52	CD80	CD86	cytotoxic T-lymphocyte-associated protein 4 (CD152)
Common abbreviation	–	–	–	–	–	–	–	CTLA-4
HGNC, UniProt	<a href="#">CD2</a> , <a href="#">P06729</a>	<a href="#">CD3E</a> , <a href="#">P07766</a>	<a href="#">MS4A1</a> , <a href="#">P11836</a>	<a href="#">CD33</a> , <a href="#">P20138</a>	<a href="#">CD52</a> , <a href="#">P31358</a>	<a href="#">CD80</a> , <a href="#">P33681</a>	<a href="#">CD86</a> , <a href="#">P42081</a>	<a href="#">CTLA4</a> , <a href="#">P16410</a>
Selective inhibitors	–	–	–	–	–	<a href="#">abatacept</a> [84], <a href="#">belatacept</a> [16]	<a href="#">abatacept</a> [84], <a href="#">belatacept</a> [16]	–
Selective antagonists	<a href="#">alefacept</a> (Inhibition) [56, 89]	–	–	–	–	–	–	–
Antibodies	–	<a href="#">catumaxomab</a> (Binding) [46], <a href="#">muromonab-CD3</a> (Binding) [24], <a href="#">otelixizumab</a> (Binding) [7]	<a href="#">ofatumumab</a> (Binding) ( $pK_d$ 9.9) [47], <a href="#">rituximab</a> (Binding) ( $pK_d$ 8.5) [78], <a href="#">ibritumomab tiuxetan</a> (Binding), <a href="#">obinutuzumab</a> (Binding) [2, 68], <a href="#">tositumomab</a> (Binding)	<a href="#">lintuzumab</a> (Binding) ( $pK_d$ ~10) [8], <a href="#">gemtuzumab ozogamicin</a> (Binding) [6]	<a href="#">alemtuzumab</a> (Binding) [22]	–	–	<a href="#">ipilimumab</a> (Binding) ( $pK_d$ > 9) [28], <a href="#">tremelimumab</a> (Binding) ( $pK_d$ 8.9) [30]

Nomenclature	<a href="#">programmed cell death 1 (CD279)</a>
Common abbreviation	PD-1
HGNC, UniProt	<a href="#">PDCD1</a> , <a href="#">Q15116</a>
Antibodies	<a href="#">pembrolizumab</a> (Binding) ( $pK_d \sim 10$ ) [9], <a href="#">nivolumab</a> (Binding) ( $pK_d$ 9.1) [29, 42, 43]
Comments	The endogenous ligands for human PD-1 are programmed cell death 1 ligand 1 (PD-L1 <i>aka</i> <a href="#">CD274</a> ( <a href="#">CD274</a> , <a href="#">Q9NZQ7</a> )) and programmed cell death 1 ligand 2 (PD-L2; <a href="#">PDCD1LG2</a> ). These ligands are cell surface peptides, normally involved in immune system regulation. Many types of cancer cells evolve mechanisms to evade control and elimination by the immune system. Such mechanisms can include inhibition of so-called 'immune checkpoints', which would normally be involved in the maintenance of immune homeostasis. An increasingly important area of clinical oncology research is the development of new agents which impede these evasion techniques, thereby switching immune vigilance back on, and effecting immune destruction of cancer cells. Three molecular targets of checkpoint inhibitors which are being extensively pursued are cytotoxic T-lymphocyte antigen 4 ( <a href="#">CTLA4</a> ), programmed cell death 1 ( <a href="#">PD-1</a> ), and programmed cell death ligand 1 (PD-L1). Using antibody-based therapies targeting these pathways, clinical responses have been reported in various tumour types, including melanoma, renal cell carcinoma [64] and non-small cell lung cancer [39, 51]. <a href="#">pembrolizumab</a> is the first-in-class, anti-PD-1 antibody to be approved by the US FDA, with ongoing clinical trials for <a href="#">nivolumab</a> (e.g. <a href="#">NCT01673867</a> , <a href="#">NCT01721746</a> ) and <a href="#">pidilizumab</a> ( <a href="#">NCT02077959</a> , <a href="#">NCT01952769</a> ).

## Methyllysine reader proteins

Other protein targets → [Chromatin-interacting transcriptional repressors](#) → [Methyllysine reader proteins](#)

**Overview:** Methyllysine reader proteins bind to methylated proteins, such as histones, allowing regulation of gene expression.

Nomenclature	<a href="#">I(3)mbt-like 3 (Drosophila)</a>
HGNC, UniProt	<a href="#">L3MBTL3</a> , <a href="#">Q96JM7</a>
Selective agonists	<a href="#">UNC1215</a> ( $pK_d$ 6.9) [38]

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## Cytokines and growth factors

Other protein targets → Cytokines and growth factors

**Overview:** cytokines and growth factors are a group of small proteins released from cells, which act upon the same cell or neighbouring cells, often with a role in immune regulation and/or proliferation. Listed herein are examples of cytokines and growth factors targeted for therapeutic benefit.

Nomenclature	interleukin 1, beta	tumor necrosis factor	vascular endothelial growth factor A
HGNC, UniProt	<i>IL1B</i> , P01584	<i>TNF</i> , P01375	<i>VEGFA</i> , P15692
Antagonists	–	–	afibercept (Inhibition) [10, 11, 82]
Selective antagonists	–	etanercept (Inhibition) [18, 23]	pegaptanib (Inhibition) [26, 61]
Antibodies	gevokizumab (Binding) ( $pK_d$ 12.5) [36, 53, 71], canakinumab (Binding) ( $pK_d$ 10.5) [27], rilonacept (Binding) [32, 55]	golimumab (Inhibition) ( $pIC_{50}$ 10.7) [77], infliximab (Inhibition) ( $pK_d$ 8.7) [44], adalimumab (Inhibition) ( $pK_d$ >8) [75], certolizumab pegol (Inhibition) [60]	ranibizumab (Inhibition) ( $pK_d$ ~9.8) [3], bevacizumab (Inhibition) ( $pIC_{50}$ 8–8.3) [3]

## Fatty acid-binding proteins

Other protein targets → Fatty acid-binding proteins

**Overview:** Fatty acid-binding proteins are low molecular weight (100–130 aa) chaperones for long chain fatty acids, fatty acyl CoA esters, eicosanoids, retinols, retinoic acids and related metabolites and are usually regarded as being responsible for allowing the oth-

erwise hydrophobic ligands to be mobile in aqueous media. These binding proteins may perform functions extracellularly (e.g. in plasma) or transport these agents; to the nucleus to interact with nuclear receptors (principally PPARs and retinoic acid receptors

[76]) or for interaction with metabolic enzymes. Although sequence homology is limited, crystallographic studies suggest conserved 3D structures across the group of binding proteins.

Nomenclature	fatty acid binding protein 1, liver	fatty acid binding protein 2, intestinal	fatty acid binding protein 3, muscle and heart	fatty acid binding protein 4, adipocyte	fatty acid binding protein 5 (psoriasis-associated)
HGNC, UniProt	<i>FABP1</i> , P07148	<i>FABP2</i> , P12104	<i>FABP3</i> , P05413	<i>FABP4</i> , P15090	<i>FABP5</i> , Q01469
Rank order of potency	stearic acid, oleic acid > palmitic acid, linoleic acid > arachidonic acid, $\alpha$ -linolenic acid [69]	stearic acid > palmitic acid, oleic acid > linoleic acid > arachidonic acid, $\alpha$ -linolenic acid [69]	stearic acid, oleic acid, palmitic acid > linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [69]	oleic acid, palmitic acid, stearic acid, linoleic acid > $\alpha$ -linolenic acid, arachidonic acid [69]	–
Comments	A broader substrate specificity than other FABPs, binding two fatty acids per protein [83].	Crystal structure of the rat FABP2 [74].	Crystal structure of the human FABP3 [87].	–	Crystal structure of the human FABP5 [33].

Nomenclature	fatty acid binding protein 6, ileal	fatty acid binding protein 7, brain	peripheral myelin protein 2	fatty acid binding protein 9, testis	fatty acid binding protein 12
HGNC, UniProt	<a href="#">FABP6</a> , <a href="#">P51161</a>	<a href="#">FABP7</a> , <a href="#">O15540</a>	<a href="#">PMP2</a> , <a href="#">P02689</a>	<a href="#">FABP9</a> , <a href="#">Q0Z7S8</a>	<a href="#">FABP12</a> , <a href="#">A6NFH5</a>
Comments	Able to transport bile acids [88].	Crystal structure of the human FABP7 [4].	<i>In silico</i> modelling suggests that FABP8 can bind both fatty acids and cholesterol [50].	–	–

Nomenclature	retinol binding protein 1, cellular	retinol binding protein 2, cellular	retinol binding protein 3, interstitial	retinol binding protein 4, plasma	retinol binding protein 5, cellular
HGNC, UniProt	<a href="#">RBP1</a> , <a href="#">P09455</a>	<a href="#">RBP2</a> , <a href="#">P50120</a>	<a href="#">RBP3</a> , <a href="#">P10745</a>	<a href="#">RBP4</a> , <a href="#">P02753</a>	<a href="#">RBP5</a> , <a href="#">P82980</a>
Rank order of potency	–	stearic acid > palmitic acid, oleic acid, linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [70]	–	–	–

Nomenclature	retinol binding protein 7, cellular	retinaldehyde binding protein 1	cellular retinoic acid binding protein 1	cellular retinoic acid binding protein 2
HGNC, UniProt	<a href="#">RBP7</a> , <a href="#">Q96R05</a>	<a href="#">RLBP1</a> , <a href="#">P12271</a>	<a href="#">CRABP1</a> , <a href="#">P29762</a>	<a href="#">CRABP2</a> , <a href="#">P29373</a>
Rank order of potency	–	11- <i>cis</i> -retinal, 11- <i>cis</i> -retinol > 9- <i>cis</i> -retinal, 13- <i>cis</i> -retinal, 13- <i>cis</i> -retinol, all- <i>trans</i> -retinal, retinol [14]	tretinoin > alitretinoin stearic acid > palmitic acid, oleic acid, linoleic acid, $\alpha$ -linolenic acid, arachidonic acid [70]	–

**Comments:** Although not tested at all FABPs, [BMS309403](#) exhibits high affinity for FABP4 (pIC50 8.8) compared to FABP3 or FABP5 (pIC50 <6.6) [20, 81]. [HTS01037](#) is reported to interfere with FABP4 action [31]. Multiple pseudogenes for the FABPs have been identified in the human genome.

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# Sigma receptors

Other protein targets → Sigma receptors

**Overview:** Although termed ‘receptors’, the evidence for coupling through conventional signalling pathways is lacking. Initially described as a subtype of opioid receptors, there is only a modest pharmacological overlap and no structural convergence with the G protein-coupled receptors. A wide range of compounds, ranging from psychoactive agents to antihistamines, have been observed to bind to these sites, which appear to be intracellular.

Nomenclature	sigma non-opioid intracellular receptor 1	$\sigma 2$
HGNC, UniProt	<a href="#">SIGMAR1</a> , <a href="#">Q99720</a>	–
Agonists	–	<a href="#">PB-28</a> (pK <sub>i</sub> 8.3) [ <a href="#">5</a> ], <a href="#">1,3-ditolyguanidine</a> (pK <sub>i</sub> 7.4) [ <a href="#">45</a> ] – Guinea pig
(Sub)family-selective agonists	<a href="#">(RS)-PPCC</a> (pK <sub>i</sub> 8.8) [ <a href="#">67</a> ]	–
Selective agonists	<a href="#">PRE-084</a> (pIC <sub>50</sub> 7.4) [ <a href="#">80</a> ], <a href="#">(+)-SK&amp;F10047</a>	–
Antagonists	<a href="#">(-)-pentazocine</a>	<a href="#">SM 21</a> (pIC <sub>50</sub> 7.2) [ <a href="#">48</a> ]
Selective antagonists	<a href="#">NE-100</a> (pIC <sub>50</sub> 8.4) [ <a href="#">62</a> ], <a href="#">BD-1047</a> (pIC <sub>50</sub> 7.4) [ <a href="#">54</a> ]	–
Labelled ligands	<a href="#">[<sup>3</sup>H]pentazocine</a> (Agonist)	<a href="#">[<sup>3</sup>H]-di-o-tolylguanidine</a> (Agonist)
Comments	–	There is no molecular correlate of the $\sigma 2$ receptor.

**Comments:** [\(-\)-pentazocine](#) also shows activity at opioid receptors.

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# Tubulins

Other protein targets → Tubulins

**Overview:** Tubulins are a family of intracellular proteins most commonly associated with microtubules, part of the cytoskeleton. They are exploited for therapeutic gain in cancer chemotherapy as targets for agents derived from a variety of natural products: taxanes, colchicine and vinca alkaloids. These are thought to act primarily through  $\beta$ -tubulin, thereby interfering with the normal processes of tubulin polymer formation and disassembly.

Nomenclature	tubulin, alpha 1a	tubulin, alpha 4a	tubulin, beta class I	tubulin, beta 3 class III	tubulin, beta 4B class IVb	tubulin, beta 8 class VIII
HGNC, UniProt	<a href="#">TUBA1A</a> , <a href="#">Q71U36</a>	<a href="#">TUBA4A</a> , <a href="#">P68366</a>	<a href="#">TUBB</a> , <a href="#">P07437</a>	<a href="#">TUBB3</a> , <a href="#">Q13509</a>	<a href="#">TUBB4B</a> , <a href="#">P68371</a>	<a href="#">TUBB8</a> , <a href="#">Q3ZCM7</a>
Inhibitors	–	–	<a href="#">vinblastine</a> (pIC <sub>50</sub> 9), <a href="#">vincristine</a>	–	–	–
(Sub)family-selective inhibitors	–	–	<a href="#">eribulin</a> (pIC <sub>50</sub> 8.2) [ <a href="#">59</a> ], <a href="#">paclitaxel</a> (Mitotic cell cycle arrest in A431 cells) (pEC <sub>50</sub> 8.1) [ <a href="#">63</a> ], <a href="#">colchicine</a> (pIC <sub>50</sub> 8) [ <a href="#">12</a> ], <a href="#">cabazitaxel</a> , <a href="#">docetaxel</a> , <a href="#">ixabepilone</a>	–	–	–

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